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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,887	07/30/2002	Jurgen Engel	103832-512-NP	6290

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,887	ENGEL ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,4 and 7-16* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,4,12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A. Formal matters

1. The amendment filed on 7/27/2005 has been made of record.

2. Claims 1-6 and 12-16 were pending. Claims 3, 5, and 6 were cancelled in the amendment filed on 7/27/2005. Therefore, claims 1, 2, 4, and 12-16 are currently pending and are considered for examination.

3. The text of those sections of Title 35, U.S.C. not included in this action can be found cited in full, in the previous office action mailed on 11/24/2004.

B. Information Disclosure Statement

The Information Disclosure Statement submitted on 4/07/2005 has been made of record and has been fully considered. The entry for the EPO communication has been lined through because it is in improper format.

C. Specification

1. Objection to the specification on the basis of improperly indicated trademarks is withdrawn in response to the Applicant's amendments. However, a rejection under 35 USC § 112, second paragraph, relating to the improper use of trademarks in the claims has been made and is outlined below.

2. The Examiner objects to the specification as having improper format. Below is a description of the contents and proper order of the contents of the specification:

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

D. 35 USC § 112, first paragraph - scope of enablement

1. Claims 1, 2, and 4, as well as dependent claims 12-16, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering sex hormone levels, does not reasonably provide enablement for defining a subject in need of treatment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The breadth of the claims is excessive with regard to lowering sex hormones for all patients in need of treatment. There are many situations in which an individual would be

in need of lowering sex hormones, including individuals with alterations/defects in T cell populations, but also individuals with hormone-dependent cancer (such as breast and prostate), reproductive disorders, and individuals undergoing birth-control therapy. Applicant provides no guidance of subjects in need of treatment other than those requiring increased T cell numbers. It would not be predictable to a person of ordinary skill in the art how to identify a subject in need of decreased sex hormone levels.

Furthermore, the specification, while being enabling for modifications of T cell populations that involve *up-regulation* of T cell numbers, does not reasonably provide enablement for any other possible modifications of T cell populations, including *down-regulation* of T cell populations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the claims read on methods of lowering sex hormones, resulting in modification of the T-cell population. On page 9 of the response dated 7/27/2005, Applicants argue that T cell levels only increase with decreasing sex hormone levels. Therefore, there is no guidance or working examples of how decreased sex hormone levels can decrease or otherwise modify T cell populations in any way other than increasing them. A person of ordinary skill in the art would interpret "modification" as being any qualitative or quantitative change in the T cell population, and the specification, while teaching up-regulation of T cell numbers, does not teach any other type of possible T cell modifications.

In summary, due to the excessive breadth of the claims and lack of guidance or working examples, it would not be predictable to a person of ordinary skill in the art how to identify patients in need of the instant invention, or how to practice any T cell modifications other than increasing the T cell populations. Thus, a skilled artisian would not know how to use the claimed invention. Therefore, because of the breath of the claims, the lack of guidance or working examples, and the unpredictability inherent in the art, the Examiner has concluded that undue experimentation would be required to practice the claimed invention.

2. Claims 1, 2, and 4, as well as dependent claims 12-16, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lowering sex hormone levels in a human subject comprising administration of peptidic LHRH antagonists such as CETRORELIX, TEVERELIX, ANTIDE, or ABARELIX, does not reasonably provide enablement for a method of lowering sex hormone levels in a human subject comprising

administration of any non-peptidic LHRH antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the instant case, the breadth of the claims is excessive because the claim are drawn to a method of lowering sex hormone levels in an individual comprising administration of any LHRH antagonist. The specification provides only minimal guidance, and provides no examples showing that any LHRH antagonist is functional in the claimed method, but recites the peptidic compounds CETRORELIX, TEVERELIX, ANTIDE, or ABARELIX as LHRH antagonists that are useful in the claimed invention. The specification also does not provide guidance or examples showing that any other potential LHRH antagonist, including any non-peptidic antagonist, as recited in claim 1, can be used in the claimed method. A person of ordinary skill in the art would not be able to predict which of many possible molecules, including small, non-peptidic molecules, could act as LHRH antagonists, and would also not be able to predict the effects of all possible molecules that could act as LHRH antagonists. Such a determination would require further, undue experimentation on the part of the skilled artisan.

In summary, due to the excessive breadth of the claims, which read on a method of lowering sex hormones comprising administration of any LHRH antagonist, including any non-peptidic LHRH antagonist, the lack of guidance and examples in the specification teaching which non-peptidic LHRH antagonists could be used, or showing that any LHRH antagonist is actually effective in the claimed method, and the unpredictability inherent in the art regarding which molecules, including non-peptidic molecules, could act as LHRH antagonists and lower sex hormones upon administration to a subject, a person of ordinary skill in the art would require further, undue experimentation to practice the claimed method commensurate with the full scope of the claims.

E. 35 USC § 112, first paragraph – written description

Claims 1, 2, 4, and 12-16 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of lowering sex hormones in a subject, wherein said method comprises administration of any LHRH antagonist. As set forth above in the 35 U.S.C. 112, first paragraph enablement rejection #2, the claims read on administration of any potential molecule, both peptidic and non-peptidic, that could function as an LHRH antagonist. Thus, the claims are drawn to a genus of molecules that is defined only by the ability to antagonize LHRH. Although the specification recites the peptidic LHRH antagonists CETRORELIX, TEVERELIX, ANTIDE, or ABARELIX, the claims are also drawn to non-peptidic LHRH antagonists. The claims do not require the non-peptidic LHRH antagonists of the instant invention to have any particular structure or composition, and there is no teaching or recitation in either the claims or the instant specification of any non-peptidic LHRH antagonist, including small molecules, chemical inhibitors, nucleotides, etc. Therefore, the claims are drawn to a genus of molecules that has not been adequately described in the specification.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the administered non-peptidic molecule(s) antagonist LHRH. There is no identification of any particular portion of any molecule that must be conserved in order to function as a non-peptidic LHRH antagonist. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of non-peptidic LHRH antagonists.

F. 35 USC § 112 – second paragraph

Rejections withdrawn

1. Rejection of claim 1 under 35 USC § 112, second paragraph, with regards to the phrase "to a certain extent", as set forth on page 4 of the prior Office Action mailed on 11/24/2004, is withdrawn in response to Applicant's amendment to remove the phrase from the claim.

2. Rejection of claims 2-6 under 35 USC § 112, second paragraph, regarding consequences of lowered sex hormone levels wherein a "modification of the T cell population" is the result, as set forth on pages 4-5 of the prior Office Action mailed on 11/24/2004, is withdrawn in response to Applicant's amendments or cancellation of claims.

3. Rejection of claims 14-16 under 35 USC § 112, second paragraph, regarding administration of LHRH antagonists based on "needs" and "as needed", as set forth on page 5 of the prior Office Action mailed on 11/24/2004, is withdrawn in response to Applicant's amendments to remove the phrases from the claims.

4. Rejection of claims 14-16 under 35 USC § 112, second paragraph, regarding a dosing regimen of LHRH that is "divided" throughout a period of time, as set forth on page 5 of the prior Office Action mailed on 11/24/2004, is withdrawn in response to Applicant's amendments to remove the phrase from the claims.

Maintained rejections/New grounds of rejection

5. Claims 14-16 are rejected under 35 USC § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims read on "optionally repeating method of lowering sex hormones". As written, the claims are missing essential method steps because they can be interpreted as reading on any method that lowers sex hormones. The Examiner suggests amending the claims to read on "optionally repeating *said* method of lowering sex hormones."

6. Claims 12-13 and 15-16 are rejected under 35 USC § 112, second paragraph, regarding the recitation of the trademark/trade names Cetrorelix, Teverelix, Antide, and Abarelix. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the

trademark/trade name is used to identify/describe various LHRH antagonists and, accordingly, the identification/description is indefinite.

G. 35 USC § 102

Rejections withdrawn

1. Rejection of claim 4 under 35 USC § 102(b) as being anticipated by Engel et al (WO 98/10781), as set forth in the prior Office Action mailed on 11/24/2004, is withdrawn in response to the Applicant's amendment to delete the term "benign prostatic hyperplasia" from the claim.

Maintained rejections/New grounds of rejection

2. Claims 1, 2, and 12-16 remain rejected under 35 USC § 102(b), as being anticipated by Engel *et al* (WO 98/10781), as set forth on pages 5-6 of the prior Office Action mailed on 11/24/2004. Engel et al teach that Cetrorelix treatment is capable of lowering sex hormones to levels above the point of castration (Figure 1 and p. 8, lines 6-8), and teaches specific doses that are encompassed by the claimed doses of the instant invention. The Applicants argue that rejection under 35 USC § 102(b) is improper because Engel *et al* does not teach each and every limitation of the claims, namely the ability of LHRH antagonists to modify T cell populations. This argument has been fully considered, but is not deemed persuasive. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer (Altas Powder Co. v Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999)). Thus, the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not necessarily make the claim patentable (In re Best, 562 F2.d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)). In the instant case, Zakharova *et al* (*Biochemistry (Mosc.),* 2000, 65(10):1135-1139) teach that LHRH antagonists are capable of modifying T cell populations. A chemical composition, in this case LHRH antagonists, and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present (in re Spada, 911 F2.d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)). In other words, the ability to modify T cell populations in inherently present in the LHRH antagonist compositions taught by Engel *et al.* Finally, Zakharova *et al* is not being used as new grounds of rejection, but to support the

Examiner's position of what was well known in the art, and inherent at the time of the present invention.

3. Claims 1 and 2 remain rejected under 35 USC § 102(b) as being anticipated by Zakharova *et al*, as set forth on page 6 of the prior Office Action mailed on 11/24/2004. Zakharova *et al* teaches that LHRH antagonists can modify T cell populations by decreasing thymocyte (T cell) proliferation. The Applicants argue that Zakharova *et al* does not teach each and every limitation of the claims. As discussed above, compounds such as LHRH antagonists have inherent features that were present at the time of invention of the instant application. In this case, while the ability of LHRH antagonists to lower sex hormone levels is not specifically taught by Zakharova *et al*, such properties are inherently present, as disclosed by Engel *et al* (see above), and also by Gonzalez-Barcena *et al* (*The Prostate*, 1994, 24:89-92), which teaches lowering of sex hormone levels by LHRH antagonists (Cetrorelix). It should be noted that Gonzalez-Barcena *et al* is not being used as new grounds of rejection, but to support the Examiner's position of what was well known in the art, and inherent at the time of the present invention.

H. 35 USC § 103

Maintained rejections/New grounds of rejection

Claims 1, 2, 4, and 12-16 are rejected under 35 USC § 103 as being unpatentable over Engel *et al* (WO 98/10781) in view of Zakharova *et al*, and further in view of Jacobson *et al* (Endocrinology, 1994, 134(6): 2516-2523). Engel *et al* describes a method for lowering sex hormone levels, but does not specifically teach modification of T cell populations or treatment of autoimmune disease. Zakharova *et al* show that LHRH antagonists are capable of altering the T cell population of an individual. Jacobson *et al* describe a method for treating an autoimmune disease, lupus, using GnRH/LHRH antagonists.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to implement the teachings of Engel *et al* in view of Zakharova *et al*, where Engel *et al* teaches a method of using LHRH antagonists to lower sex hormone levels, while Zakharova *et al* teaches that LHRH antagonist treatment modifies T cell populations. A person of ordinary skill in the art would have been motivated to incorporate the teachings of Engel *et al*

and Jacobson *et al* because Jacobson *et al* shows that GnRH/LHRH antagonists, including Cetrorelix, are a feasible approach for therapies directed against autoimmune disease. Furthermore, Engel *et al* describes specific doses of LHRH antagonists that are effective in lowering sex hormones to levels above the point of castration, and specifies durations of treatment (page 8, Example 1), both of which encompass the claimed dosages and treatment times of the instant invention, providing further support for the motivation to use a method of therapy directed against autoimmune disorders based on treatment with LHRH antagonists. Finally, it would also be obvious to a person of ordinary skill in the art, to combine the above teachings to use LHRH antagonists as a therapy for any disease in which modifications of T cell populations in a critical feature of disease pathogenesis, including HIV infection, cancer, arthritis, multiple sclerosis, dermatitis, and asthma.

I. Double Patenting

Rejection of claims 1-14 over 35 USC § 101, as claiming the same invention as that of claims 1-11 of copending Application No. 10/717,129, as set forth on page 8 of the prior Office Action mailed on 11/24/2004, is withdrawn due to abandonment of Application No 10/717,129.

J. Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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